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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,909	02/02/2001	Mark Roberts	M0975/7006 (JRV)	9660

7590 12/31/2002

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EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	6

DATE MAILED: 12/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/775,909	Roberts	
	Examiner	Group Art Unit	
	Duffy	1645	

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 10-7-02.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 37-54 is/are pending in the application.

Of the above claim(s) 47-54 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 37-46 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 37-54 are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☒ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

DETAILED ACTION

1. The response filed 10-7-02 has been entered into the record.

Priority

2. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

3. Acknowledgment is made of applicant's claim for foreign priority based on an applications filed in Great Britain on 10-5-93 and 12-2-93. It is noted, however, that applicant has not filed a certified copy of the Great Britain applications as required by 35 U.S.C. 119(b).

Drawings

4. The drawings are objected to for the reasons set forth on the enclosed PTO-948. A proposed drawing correction or corrected drawings are required in reply to this Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

6. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

7. This application is informal in the arrangement of the specification. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to the drawings, each of the lettered items should appear in upper case, without underling or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) Title of the Invention.

(b) Cross-Reference to Related Applications.

© Statement Regarding Federally Sponsored Research or Development.

(d) Reference to a "Sequence Listing," a table, or a computer program listing appendix submitted on compact disc (see 37 CFR 1.52(e)(5)).

(e) Background of the Invention.

1. Field of the Invention.

2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(f) Brief Summary of the Invention.

(g) Brief Description of the Several Views of the Drawing(s).

(h) Detailed Description of the Invention.

(I) Claim or Claims (commencing on a separate sheet).

(j) Abstract of the Disclosure (commencing on a separate sheet).

(k) Drawings.

(l) Sequence Listing, if on paper (see 37 CFR 1.821-1.825).

Oath/Declaration

8. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Information Disclosure Statement

9. The information disclosure statement filed 10-7-02 has been considered, an initialed copy is enclosed.

Election/Restriction

10. Claims 47-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 4.

Claim Rejections - 35 U.S.C. § 102 or 103

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 37, 38, 40, 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Capiau et al (EP 352250, published 1-24-90).

Capiau et al teaches a vaccine comprised of a double mutant pertussis toxin with a modification at the tryptophan residue at amino acid position 26. (see especially abstract). Capiau et al also discloses additional modification can be included to produce a double mutant. These modifications include mutations at the glutamic acid at amino acid position 129 or the arginine at the amino acid position 9. (see especially page 6, lines 14-37). In addition, the reference discloses a method of oral or intranasal administration of the mutant pertussis toxin to humans; the toxin can be administered alone or with other antigens such as filamentous haemagglutinin (FHA), tetanus toxoid and/or diphtheria toxoid or any other protective antigen of *Bordetella pertussis*. (see especially page 7, lines

50-56; page 8, lines 41-59). Because the pertussis toxin contains the same claimed mutations, it is innately non-toxic. Therefore, Capiau et al meets the claimed vaccination methods.

14. Claims 37-44 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Nencioni et al (Acta. Med. Rom. 29:78-83, 1991) or Podda et al (J. Exp. Med. 172:861-868, 1990) in view of Capiau et al (EP 352250, published 1-24-90), Tamura et al (U.S. Patent No. 5,182,109) and Honda et al (Japanese Application #3-135923).

Nencioni et al teaches a double mutant pertussis toxin PT-9K/129G which can be administered alone or in combination with the *Bordetella pertussis* antigens FHA and 69K. (see abstract, page 81, last paragraph, page 82, fifth paragraph).

Podda et al also teach the double mutant pertussis toxin PT-9K/129G which can be combined with the 69 kD protein and FHA. (see especially abstract; page 867, second and last paragraph).

Nencioni et al and Podda et al references differ in not teaching the double mutant toxin and antigen in the form of nasal drops or nasal spray for mucosal administration.

Capiau et al discloses double mutants pertussis toxin S1 subunit with a modification at the tryptophan residue at amino acid position 26. (see especially abstract). Capiau et al also discloses additional modification can be included to produce a double mutant. These modifications include mutations at the glutamic acid at amino acid position 129 or the arginine at the amino acid position 9. (see especially page 6, lines 14-37). In addition, the reference discloses a method of oral or intranasal administration of the mutant pertussis toxin to humans; the toxin can be administered alone or with other antigens such as filamentous haemagglutinin (FHA), tetanus toxoid and/or diphtheria toxoid or any other

protective antigen of *Bordetella pertussis*. (see especially page 7, lines 50-56; page 8, lines 41-59).

Tamura et al teach a vaccine preparation comprising a toxin (such as pertussis toxin) combined with a vaccine that can be administered intranasally in the form of a nasal spray or nose drops. The vaccine preparations can be stored in a container until needed. (see abstract, column 9 and column 17). Tamura et al teach that nasal administration has the benefit of stimulating IgA antibody production (see column 3).

Honda et al teach a method of nasal inoculation of pertussis toxin B sub-unit and a vaccine antigen in order to produce an immune response which is greater tan subcutaneous inoculation (see especially abstract, page 1; page 2, last paragraph; page 3, first and fourth paragraph; and page 4, last paragraph).

It would have been prima facie obvious at the time the invention was made to administer the double mutation of Nencioni et al and Podda et al in combination with the *Bordetella pertussis* antigens FHA and 69K by nasal administration because Honda et al teach that nasal inoculation of pertussis toxin and a vaccine antigen produces an immune response which is greater than subcutaneous administration, Tamura et al teaches that nasal administration has the benefit of inducing an IgA response and Capiau et al teach oral or intranasal administration of double mutant pertussis toxins in combination with other antigens such as FHA and such as filamentous haemagglutinin (FHA), tetanus toxoid and/or diphtheria toxoid or any other protective antigen of *Bordetella pertussis* for the protection from disease. The combined teaching so the prior art suggest to one of skill in the art that vaccines comprised of bacterial toxins such as pertussis toxin, can be administered intranasally in the form of nasal drops or nasal sprays in order to produce an greater immune response.

15. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nencioni et al (Acta. Med. Rom. 29:78-83, 1991) or Podda et al (J. Exp. Med. 172:861-868, 1990); Capiau et al (EP 352250, published 1-24-90), Tamura et al (U.S. Patent No. 5,182,109) and Honda et al (Japanees e Application #3-135923) as applied to claims 37-44 and 46 above and further in view of Halpern et al (Infection and Immunity 58(4):1004-1009, 1990).

Nencioni et al (Acta. Med. Rom. 29:78-83, 1991) or Podda et al (J. Exp. Med. 172:861-868, 1990) in view of Capiau et al (EP 352250, published 1-24-90), Tamura et al (U.S. Patent No. 5,182,109) and Honda et al (Japanese Application #3-135923) as combined is set forth supra. The method as combined differ in not teaching the combination of the double mutant with fragment C antigen of tetanus toxin.

Halpern et al teach that Fragment C can be a suitable alternative to tetanus toxin in many applications (see especially abstract). Halpern et al also teach that the C fragment antigen retains the activity of the intact tetanus toxin avoiding the need to use the intact tetanus toxin with requires toxioding. Halpern et al also tech a method of immunizing mice with Fragment C to product antibodies.

It would have been prima facie obvious to one of ordinary skill in the art at the time that the invention was made to modify the nasal vaccine as combined by adding Fragment C according to Halpern into the nasal vaccine as combined above and nasally administering the vaccine as so modified because Capiau et al teach that the double mutant pertussis toxin can be combined with tetanus toxoid and Halpern et al teach that Fragment C has the benefits of inducing an appropriate immune response and provides the benefit of not having to make a toxoid of the toxin. One would have been motivated to include Fragment C of Halpern et al to provide additional protection against tetanus while avoiding the use of intact toxins which would require toxoiding.

Status of Claims

16. No claims are allowed.

17. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 10:00 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
December 19, 2002

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600